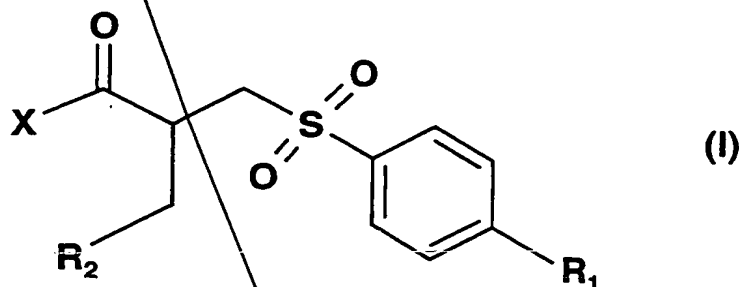


CLAIMS

1. A compound which is a 3-arylsulfonyl-2-methyl propanoic acid derivative of formula (I):

5



wherein

X is HO-NH- or HO-;

- 10 R<sub>1</sub> is selected from phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-cyanophenyl, benzamido (i.e., -NH-CO-Ph) and benzamido substituted on the terminal phenyl ring by C<sub>1</sub>-C<sub>4</sub> alkyl, fluoro, chloro, cyano or C<sub>1</sub>-C<sub>4</sub> alkoxy;

R<sub>2</sub> is selected from:

- 15 (a) -S-Ar or -S-CH<sub>2</sub>-Ar wherein Ar is a monocarbocyclic or bicarbocyclic aromatic moiety which is either unsubstituted or substituted with one or two substituents selected from C<sub>1</sub>-C<sub>4</sub> alkyl, phenyl, benzyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, fluoro, chloro, bromo, nitro, cyano, hydroxy, amino, dimethylamino, acetamido, methylthio and acetyl;

(b) -O-Ar, wherein Ar is as defined above;

- 20 (c) -S-Het or -S-CH<sub>2</sub>-Het, wherein Het is a heterocyclic ring selected from pyridine, pyrimidine, pyridazine, pyrazine, 1,2,5-triazine, imidazole, thiophene, furan, pyrrole, pyrazole, 1,3-thiazole, 1,3-oxazole, 1,2,3-triazole, 1,2,4-triazole, 1,3,4-thiadiazole, 1,3,4-oxadiazole, 1,2,3,4-tetrazole, quinoline, isoquinoline, indole, 1,3-benzoxazole, 1,3-benzothiazole, benzimidazole, [1,3]oxazolo[4,5-b]pyridine, [1,3]thiazolo[4,5-b]pyridine, [1,2,3,4]tetrazolo[1,5-b]pyridazine and purine, and wherein said Het group can be  
25 substituted with one to three substituents selected from C<sub>1</sub>-C<sub>4</sub> alkyl, phenyl, pyridyl,

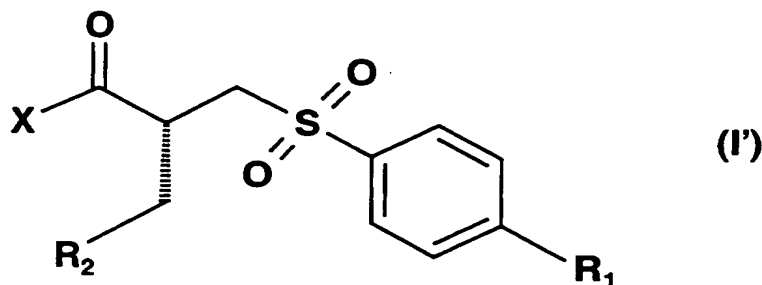
Sub  
A'

Sub  
A1  
benzyl, C<sub>1-4</sub> alkoxy, methylthio, fluoro, chloro, nitro, cyano, hydroxy, oxo, amino, methylamino, dimethylamino, 2-dimethylaminoethyl, acetamido and acetyl; and

(d) 2,5-dioxo-1-imidazolidinyl or 2,4-dioxo-1-imidazolidinyl, either of which is optionally substituted at the carbon atom by one or two methyl, linear or branched C<sub>2</sub>-C<sub>4</sub> alkyl, phenyl, benzyl or hydroxymethyl groups, and at the nitrogen atom with C<sub>1</sub>-C<sub>4</sub> linear or branched alkyl;

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 which is an isomer having the configuration depicted in formula (I'):



15 wherein X, R<sub>1</sub> and R<sub>2</sub> are as defined in claim 1.

3. A compound according to claim 1 which is selected from:

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

(2S)-3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[[(4-hydroxyphenyl)sulfanyl]methyl]propanoic

acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[[[(4-hydroxyphenyl)sulfanyl]-

- methyl]propanamide;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-(phenoxymethyl)propanoic acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-(phenoxymethyl)propanamide;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-pyridinylsulfanyl)methyl]propanoic
- 5 acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(2-pyridinylsulfanyl)methyl]-propanamide;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[2-(2-pyridinylmethyl)sulfanyl]methyl]-propanoic acid;
- 10 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[[2-(2-pyridinylmethyl)sulfanyl]methyl]propanamide;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[5-(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]methyl]propanoic acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[[5-(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]methyl]propanamide;
- 15 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[5-(5-amino-1,3,4-thiadiazol-2-yl)sulfanyl]methyl]propanoic acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[1-(1-methyl-1H-imidazol-2-yl)sulfanyl]methyl]propanoic acid;
- 20 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-pyrimidinylsulfanyl)methyl]propanoic acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[1-(1-methyl-1H-tetrazol-5-yl)sulfanyl]methyl]-propanoic acid;
- 25 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[1-(1-benzyl-1H-tetrazol-5-yl)sulfanyl]methyl]-propanoic acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(1H-benzimidazol-2-ylsulfanyl)methyl]-propanoic acid;
- 30 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(1,3-thiazol-2-ylsulfanyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[2-methyl-2H-1,2,3-triazol-4-yl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[5-phenyl-1,3,4-oxadiazol-2-yl)sulfanyl]-methyl]propanoic acid;

5 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[[1-(3-pyridinyl)-1H-imidazol-2-yl)sulfanyl]-

methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[4-methyl-1,3-oxazol-2-yl)sulfanyl]methyl]-

10 propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[1,3]oxazolo[4,5-b]pyrimidin-2-yl)sulfanyl]-

methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[1,2,3,4]tetrazolo[1,5-b]pyridazin-6-yl)sulfanyl]methyl]propanoic acid;

15

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[2,6-dimethyl-4-pyrimidinyl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[4,6-dimethyl-2-pyrimidinyl)sulfanyl]-methyl]propanoic acid;

20 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[4-hydroxy-6-methyl-2-pyrimidinyl)sulfanyl]methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[4,6-dihydroxy-2-pyrimidinyl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(9H-purin-6-yl)sulfanyl]methyl]propanoic acid;

25

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-(3-fluorophenoxymethyl)propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-acetylaminophenoxy)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(4-acetylaminophenoxy)methyl]propanoic acid;

30

3-[[1,1'-Biphenyl]-4-yl)sulfonyl]-2-[(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl]-

- propanoic acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)-methyl]propanoic acid;
- 5 (2R)-3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl]propanoic acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl]propanamide;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)-methyl]propanoic acid;
- 10 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)methyl]propanamide;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2,5-dioxo-1-imidazolidinyl)methyl]propanoic acid;
- 15 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(2,5-dioxo-1-imidazolidinyl)methyl]propanamide;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-methyl-2,5-dioxo-1-imidazolidinyl)-methyl]propanoic acid;
- 20 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-ethyl-2,5-dioxo-1-imidazolidinyl)methyl]-propanoic acid;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-butyl-2,5-dioxo-1-imidazolidinyl)methyl]-propanoic acid;
- 25 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(3-butyl-2,5-dioxo-1-imidazolidinyl)methyl]propanamide;
- 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-butyl-2,4-dioxo-1-imidazolidinyl)methyl]-propanoic acid;
- 30 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(3-butyl-2,4-dioxo-1-

imidazolidinyl)methyl]propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(5-isopropyl-2,4-dioxo-1-imidazolidinyl)-methyl]propanoic acid;

5 3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(5-hydroxymethyl-2,4-dioxo-1-imidazolidinyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(5-hydroxymethyl-3-methyl-2,4-dioxo-1-imidazolidinyl)methyl]propanoic acid;

3-[(4'-Fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

10 3-[(4'-Fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[(4'-Fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[(4'-Fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-(phenoxymethyl)propanamide;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

15 3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-(phenoxymethyl)propanamide;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-(3-fluorophenoxymethyl)propanoic acid;

20 3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-acetylamino)phenoxymethyl]propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-pyridinylsulfanyl)methyl]propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[[(2-pyridinylmethyl)sulfanyl]methyl]-propanoic acid;

25 3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-butyl-2,5-dioxo-1-imidazolidinyl)methyl]-propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(3-butyl-2,5-dioxo-1-imidazolidinyl)methyl]propanamide;

30 3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(5-hydroxymethyl-2,4-dioxo-1-imidazolidinyl)methyl]propanoic acid;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-  
propanamide;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-2-[[2-(pyridinylmethyl)sulfanyl)methyl]propanoic  
acid;

5 3-[[4-(Benzoylamino)phenyl]sulfonyl]-2-[(2-thienylsulfanyl)methyl]propanoic acid;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[[4-[(4-Methylbenzoyl)amino]phenyl]sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic  
acid;

10 3-[[4-[(4-Methylbenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-  
propanamide;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic  
acid;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-  
propanamide;

15 3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-(phenoxymethyl)-  
propanamide;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-(3-fluorophenoxymethyl)propanoic  
acid;

20 3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-[[2-(pyridinylmethyl)sulfanyl)methyl]-  
propanoic acid;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-[[1-methyl-1H-tetrazol-5-yl)sulfanyl]-  
methyl]propanoic acid;

25 3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-[(5-hydroxymethyl-2,4-dioxo-1-  
imidazolidinyl)methyl]propanoic acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic  
acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-  
propanamide;

30 3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-[[1-methyl-1H-tetrazol-5-yl)sulfanyl]-  
methyl]propanoic acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-(phenoxymethyl)-  
propanamide;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-(3-fluorophenoxymethyl)propanoic  
5 acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-(3-fluorophenoxymethyl)-  
propanamide;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-[(2-acetylamino)phenoxymethyl]-  
propanoic acid;

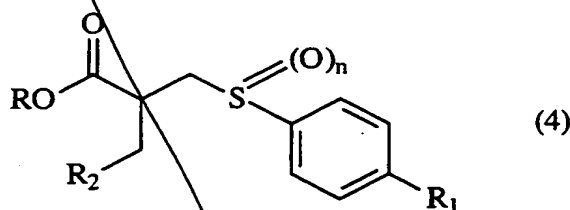
10 3-[[4-(4-Propylbenzoylamino)phenyl]sulfonyl]-2-[[[(1-methyl-1H-tetrazol-5-yl)sulfanyl]-  
methyl]propanoic acid; and

3-[[4-[(4-Methoxybenzoyl)amino]phenyl]sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[2-(hydroxymethyl)phenoxy]methyl]-  
propanoic acid; and the pharmaceutically acceptable salts thereof.

15

4. A process for producing a compound as defined in claim 1, starting from a  
compound of formula 4:



20

wherein R is H or the residue of a carboxylic acid ester, R<sub>1</sub> and R<sub>2</sub> are as defined in  
claim 1 and n is 0 or 2, which process comprises:

(a) hydrolysing a said compound of formula 4 in which R is the residue  
of a carboxylic and ester to give a compound of formula (I) in which X is HO-; or

(b) hydrolysing and oxidising, in either order, a said compound of  
25 formula 4 in which n is 0 and R is the residue of a carboxylic acid ester, to give a  
compound of formula (I) in which X is HO-; or



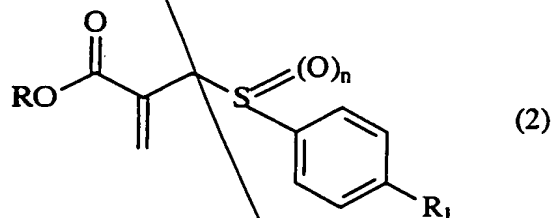
(c) activating a said compound of formula 4 wherein R is H and n is 2 to form an activated carboxy group, coupling the activated carboxy group with hydroxylamine or an O-protected derivative thereof and, if necessary, deprotecting the hydroxamic group to give a compound of formula (I) wherein X is -NHOH; or

5 (d) submitting a said compound of formula 4 wherein R is H and n is zero to a sequence of reactions comprising oxidation at the sulphur atom, activation of the carboxy group, condensation of the activated carboxy group with hydroxylamine or an O-protected derivative thereof and, if necessary, deprotection of the hydroxamic group to form a compound of formula (I) wherein X is -NHOH, the oxidation step being conducted  
10 either before the activation step or after the condensation step; and/or

(e) if desired, converting a resulting compound of formula (I) into another compound of formula (I); and/or converting a free compound into a pharmaceutically acceptable salt thereof; and/or converting a salt into a free compound.

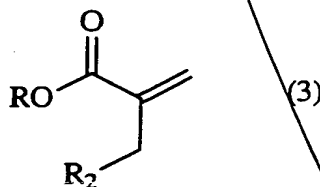
15 5. A process according to claim 4 wherein the compound of formula 4 is obtained by

(a) subjecting a compound of formula 2:



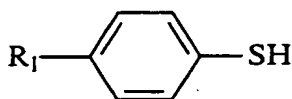
20 wherein R, R<sub>1</sub> and n are as defined in claim 4, to conjugate addition by treatment with a compound of formula R<sub>2</sub>H wherein R<sub>2</sub> is as defined in claim 1; or

(b) treating a compound of formula 3:



wherein R and R<sub>2</sub> are as defined in claim 4, with a thiol of formula:

Sub  
A2



to obtain a compound of formula 4 in which n is zero.

- 5 6. A pharmaceutical composition which comprises a pharmaceutically acceptable carrier or diluent and, as an active principle, a compound as defined in any one of claims 1 to 4.

7. A compound as defined in any one of claims 1 to 4, for use in a method of  
10 treatment of the human or animal body by therapy.

8. A compound as claimed in claim 7 for use in the treatment or prophylaxis of a disease in a mammal mediated by a matrix metalloproteinase.

- 15 9. A compound as claimed in claim 8 wherein the matrix metalloproteinase is a gelatinase (MMP-2), the membrane-type MMP involved in gelatinase activation (MMP-14), a stromelysin (MMP-3 or MMP-10), collagenase (MMP-13) or neutrophil collagenase (MMP-8).

- 20 10. A compound as claimed in any one of claims 7 to 9 for use in the treatment or prophylaxis of tumour growth or metastasis, rheumatoid arthritis, osteoarthritis, ophthalmic disease, cardiovascular disease, periodontal disease, multiple sclerosis or Alzheimer's disease.

add  
A3